

## II. REMARKS:

### A. Status of the Claims

Claims 1-2 were originally filed with the case. Claims 3-18 were added in a Response to Office Action filed on March 9, 2005. Claims 1, 3, 4, 6, 8, 10, and 16 are amended herein to correct typographical errors, correct dependency and to clarify the subject matter of the claims. Claim 2 is canceled herein. Support for the amendments to the claims may be found in the specification and the claims as originally filed. Thus, claims 1, and 2-18 are currently pending.

### B. The Claims are Patentable Over U.S. Patent 5,516,522 and Clark

The Action rejects claims 1-5 and 8-18 as being obvious over U.S. Patent No. 5,516,522 (the '522 patent) and Clark. The '522 patent is said to teach prednisolone, prednisolone acetate, triamcinolone, fluoromethalone, and fluoromethalone acetate as useful in treating proliferative vitreoretinopathy and that the ocular formulation may be an intraocular implant. Clark is said to teach anecortave acetate as useful in treating ocular neovascularization. The Action acknowledges that the references taken together do not expressly teach the incorporation of both steroids and anecortave acetate together in a method of treating angiogenesis disorders, nor do they teach the claimed dosages. Applicants respectfully traverse.

The '522 patent appears to describe a biodegradable drug delivery device designed to solve the problem of prolonged drug release into the vitreous of the eye that does not have to be removed after delivery of all of the drug in the device. While the '522 patent mentions the potential use of steroids in the device described therein, it does not provide any teaching or suggestion of dosage amounts of particular steroids for the treatment of pathologic ocular

angiogenesis. Nor does the '522 patent contain any mention of the use of anecortave acetate with the steroids for the treatment of pathologic ocular angiogenesis.

Determining obviousness requires an analysis of the invention *as a whole*. *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 724 (Fed. Cir. 1990). Significantly, *Gillette* emphasizes that whether all of the elements of the claimed invention were old in other contexts is immaterial to the issue of obviousness. Rather, "*what must be found obvious to defeat the patent is the claimed combination.*" *Id.* (quoting *Kimberly-Clark Corp. v. Johnson & Johnson*, 745 F.2d 1437, 1448, 223 U.S.P.Q. 603, 609-10 (Fed. Cir. 1984)) (emphasis in original). The '522 patent describes a biodegradable drug delivery device from which numerous compounds may be delivered. The fact that steroids for the treatment of proliferative vitreoretinopathy are included in that long list and that a separate reference describes the use of anecortave acetate for treating ocular neovascularization does not, in itself, make obvious the combination for treating pathologic ocular angiogenesis.

It is well settled patent law that "obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art." *See In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992); MPEP § 2143.01. Furthermore, the fact that a reference or references can be combined or modified is not sufficient to establish obviousness. For example, the Federal Circuit held in *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990), that the mere fact that combination or modification of a reference or references is possible does not establish obviousness of the resultant combination unless the prior art also suggests the desirability of the

combination, *i.e.*, unless the prior art provides motivation to produce the resultant combination. *Mills*, 16 U.S.P.Q.2d at 1432; *see also* MPEP § 2143.01, page 2100-91.

Moreover, the Board of Patent Appeals and Interferences has held that the fact that the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish obviousness. *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (BPAI 1993). The Action's reasoning with respect to motivation boils down to a statement that it would have been obvious to combine the two compounds because they were already individually known and it would have been within the skill of the artisan to determine the dosage amounts. This reasoning is the same reasoning that the court warns against in its holdings in *Levengood*, *Gillette*, and *Mills*. Focusing on the obviousness of substitutions and differences, instead of on the invention as a whole, is a legally improper way to simplify the often difficult determination of obviousness. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1383, 231 USPQ 81, 93 (Fed.Cir.1986), cert. denied, > 480 U.S. 947, 107 S.Ct. 1606, 94 L.Ed.2d 792 (1987).

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection based upon the '522 patent and Clark be withdrawn.

**C. The Claims are Patentable Over WO95/03807 and Clark**

The Action rejects claims 1-2, 4-5 and 16-18 as being unpatentable over WO 95/03807 ('807) and Clark. Reference '807 is said to teach a method of treating neovascular macular degeneration by administration of triamcinolone and that the drug may be administered by intravitreal injection. Clark is said to teach a method of treating ocular neovascularization

disorders using anecortave acetate. The Action acknowledges that the references taken together do not teach the incorporation of both the triamcinolone and anecortave acetate together in a method of treating angiogenesis disorders. The Action asserts that it would have been obvious to incorporate triamcinolone and anecortave acetate together in a method of treating angiogenesis disorder. Applicants respectfully traverse.

As with the rejection discussed above, the rejection of the claims as being obvious over the '807 reference and Clark amounts to a statement that it would have been obvious to combine the two compounds for the treatment of pathologic ocular angiogenesis because each compound was known separately. Applicants arguments provided above with respect to the obviousness rejection based upon the '522 patent and Clark apply equally with respect to the rejection based on the '807 reference and Clark. Neither reference mentions the claimed combination for the treatment of pathologic ocular angiogenesis, as the Action admits. According to the established caselaw, a clear explanation of the motivation for the combination is required in order to establish obviousness. That explanation has not been provided.

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection based on the '807 reference and Clark be withdrawn.

**D. The Claims are Patentable Over Clark and U.S. Patent No. 4,686,214**

The Action next rejects claims 1-3 and 6-7 as being unpatentable over Clark and U.S. Patent No. 4,686,214 (the '214 patent). The '214 patent is said to teach rimexolone as useful in treating ocular inflammation. The '214 patent is further said to teach an effective dosage for rimexolone of 0.05 to 2.0%. Clark is said to teach that anecortave acetate is useful in

treating ocular neovascularization inflammatory conditions. The Action acknowledges that the references taken together do not teach the incorporation of both rimexolone and anecortave acetate together in a method of treating angiogenesis inflammatory disorders. Nevertheless, the Action asserts that it would have been obvious to combine rimexolone and anecortave acetate to treat angiogenesis inflammatory disorders. Applicants respectfully traverse.

Once again, the Action's reasoning amounts to a statement that the claimed combination would have been obvious because each compound was known separately. Once again, there is no teaching within either cited reference to suggest the combination or to motivate the skilled artisan to make the claimed combination. The Action admits that the combination of the references does not teach the claimed combination. Nevertheless, without providing explanation as to the motivation, the Action asserts that it would have been obvious to make the combination. Applicants submit that the established caselaw (*i.e.*, *Levengood*, *Gillette*, and *Mills*) requires more than a bare statement that the compounds were known separately, therefore it would have been obvious to combine them.

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection based on Clark and the '214 patent be withdrawn.

**E. Conclusion**

This is submitted to be a complete response to the outstanding Action. Based on the foregoing arguments, the claims are believed to be in condition for allowance; a notice of allowability is therefore respectfully requested.

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The Examiner is invited to contact the undersigned attorney at (817) 551-4321 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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